Analytical Goals in New and Non-Traditional Clinical Laboratory Techniques

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Abstract: There can be absolutely no debate that, in the current economic and social climate, the demands on the medical care delivery system are changing. Yet, in the rush to develop faster and cheaper systems for care delivery, every effort must be made to maintain and--where possible--to improve the quality of care given to patients. The clinical laboratory serves as a very effective model for evaluating the changes and challenges associated with keeping the patient first among priorities which may sometimes be confusing and even conflicting.

Definitions of analytical quality vary somewhat depending upon the observer's point of view; it is important to affirm that none of these views is incorrect. Quality as defined by the traditional clinical laboratorian, some other analyst, the clinical care giver, or the patient will impact the appropriateness of analytical goals. Each of these definitions of quality may be correct, but each is also likely to be incomplete.

Alternative site/point of care laboratory testing strategies have been introduced to the testing armamentarium amid great confusion about how to define and assure quality. Little thought was given to analytical goals and how to achieve them before most alternative site testing strategies were introduced. A close analysis of the history of analytical goal setting in blood glucose monitoring gives insight into the ways in which analytical goal setting, monitoring, and assurance should be approached as new and diverse approaches such as nanotechnology and molecular pathology are introduced into common use.

Introduction

The delivery of medical care in the United States is changing; whether we like it or not, a variety of economic and sociopolitical forces are forcing us to reevaluate and, in some cases, to radically reengineer the manner in which we deliver care. Technological advancements, improved computer-based information management, and a consolidated systems approach should allow the clinical laboratory to survive and even to thrive under whatever delivery system evolves. The major challenge facing all players in the laboratory industry, however, will continue to be this: Putting all personal, professional, and parochial motives aside, how can we develop approaches which deliver the best possible care to our patients? Major concerns still exist regarding the part to be played by alternative site/point of care testing strategies such as bedside glucose monitoring, coagulation testing, and blood gas and electrolyte evaluation. Rapidly evolving techniques such as molecular pathology and in vivo monitoring represent special challenges in goal setting.

Developing appropriate analytical goals is heavily dependent upon the prior development, knowledge, and understanding of applicable clinical goals. Analytical goals must not be disjoined from the real world

Central Laboratory Testing	Point-of-Care Laboratory Testing
Many tests; few sites; few instruments	Few tests; many sites; many instruments
Large runs; “factory” environment	Small runs; “boutique” environment
Few highly trained analysts	Many inexperienced analysts
Analysts with restricted tasks in the testing cycle	Analysts with more general tasks in the testing cycle
Longer turnaround time	Shorter turnaround time
Controlled physical environment for reagents and instruments	Less controlled physical environment for reagents and instruments
Error types: “shifts and trends”	Error types: “sporadic”

Table 1. Comparison of analytical systems in central laboratory testing vs point-of-care laboratory testing.

application of the clinical test, lest we fall into the trap of spending unacceptable amounts of our resources searching for an analytical equivalent of the holy grail--an analytically pure and absolutely "correct" answer. The 1976 College of American Pathologists Aspen Conference on Analytical Goals in Clinical Chemistry developed a primary recommendation that analytical goals can only be defined in terms of needs for patient care,[1] a goal that is all too easy to lose sight of. Medical care is probably most effective when data are derived in approximately the following proportions: 70% from the clinical history, 20% from the physical examination, and 10% from laboratory tests.[2] The part played by the laboratory in medical decision making is important, but not preeminent. On the other hand, clinicians must also understand and be willing to adhere to appropriate clinical goals; uncritical reliance upon new technology and unnecessary focus upon speed of the results as a primary virtue must be vigorously challenged. It has been suggested that under any circumstances, faster results are preferable to slower results. This defies logic, especially if the faster results are unacceptably expensive or are incorrect.

Many of us trained in laboratories where a sign on the wall stated: "Speed, quality, and low cost--you can have any two." A major challenge in the coming environment is to change this approach, so that instead of sacrificing one or two of these desirable attributes of laboratory tests, we find systems which optimize all three. If our clinical goal may be summarized as "take good care of patients," then our analytical goal may be synthesized as follows: To get the best quality answer possible in a clinically appropriate time frame at the lowest cost attainable. Focusing on analytical quality alone as the only domain of analytical goals will no longer be acceptable.

Blood Glucose Testing

Possibly because blood glucose is a common analyte, much has been written about medical relevance and analytical goals for glucose. Additionally, glucose has presented a special challenge since it is the most frequent analyte evaluated at the bedside, through the use of glucose reflectance meters. Thus, glucose may serve as a test case for analyzing the effectiveness of implementing of alternative site testing strategies. From this case we may learn much.

Table 1 offers a contrast between the analytical systems inherent in central laboratory testing versus testing at the bedside. Although this table was developed with blood glucose testing in mind, it generalizes rather well to the range of laboratory testing done at the point of care. Each type of testing has strengths and weaknesses. Although analytical goals for in-hospital glucose testing should be the same regardless of where or how the test is done, this table helps to emphasize that the quality assurance systems appropriate to assure analytical success may well differ depending on the type of testing system. Application of the concepts of process control which are quite appropriate in the central laboratory may not be quite so appropriate for testing at the bedside. Another point to be made from evaluating these contrasting elements is the important, though different, role of the analyst in each setting. There is a need in the central laboratory to broaden the technologist's perspective so that there is more focus on the patient and less focus on the test as an end in itself; on the other hand, there is a great need to integrate the bedside analyst more into the quality evaluation of the testing process. Neither testing at the point of care nor testing in central laboratories is implicitly good or bad. Each type of testing has inherent strengths and weaknesses; each may hold specifically different requirements to assure that analytical goals are achieved.

If analytical goals are dependent upon clinical goals for relevance and if clinical goals should be more specific than just "to take good care of patients," it is useful to dwell for a moment upon the question of how clinical goals are set. In many institutions, blood glucose monitoring in the central laboratory has not significantly decreased when bedside testing has been introduced. Rather, the entrance of bedside testing has been more or less additive to the total amount of testing done. One suspects that, although clinical goals including such approaches as critical pathways and protocols of care should incorporate issues such as frequency and type of glucose testing necessary for adequate patient monitoring, they do not. This suspicion is verified by anecdotal evidence indicating that in some hospitals, blood glucose monitoring is routinely performed twice daily, in others it is performed four times daily, and in others it may be performed as often as once an hour. Critical pathways should never be so rigid as to disallow clinical judgment needed to care for patients, but one suspects that in this and many other instances we have not even begun to establish guidelines for what is necessary for good care. It is little wonder, then, that our efforts to establish appropriate analytical goals are splintered and somewhat feeble. The first step in establishing analytical goals should be articulating clinical goals; as we integrate new testing strategies into the care of patients, it is vitally important that clinical goals be established and understood. Until now we have not done very well in this regard.

Fraser has done much of the work to help us understand how analytical goals should be set.[3] Basically, goals are set biologically, experimentally, or experientially and generally have relied upon statistical evaluation of the coefficient of variation of multiple observations as a reflection of imprecision or random error. Biological goals have generally grown from the strategy of Cotlove, which holds that the allowable coefficient of variation for an analyte should be less than one half of the observed biological variation.[4] Based upon this approach, the analytical goal for blood or serum glucose may be demonstrated to be in the range of 2 to 3 percent. Experimental approaches to analytical goal setting include evaluating reference values, the state of the art, and analyzing the effect of errors on clinical decision making; experiential goal setting may reflect the opinions of clinicians or of expert committees or, in the case of glucose evaluation, may even reflect analytical goals derived from the opinions of patients themselves.[5] Each of these approaches, when applied to the glucose issue, gives a somewhat different view. Cumulatively, desirable coefficient of variation may range from 2 to 15 percent depending upon which approach is taken. It is clear that we really do not know what our analytical goal should be. This no doubt reflects our confusion about clinical goals, and is a state of affairs which is not likely to improve until more cogent clinical goals are established.

We have a number of tools at our disposal which allow us to monitor our achievement of goals; as new technologies develop and are implemented into the care of patients, it will be critically important that we use all of the quality systems which are at our disposal, since each of them will tell us something different about the sort of job we are doing. There has been a tendency to rely heavily upon data from external proficiency testing programs in discussing analytical goals; this is not inappropriate but must be supplemented with evaluation of other data such as integrated hospital quality assurance data, quality control data, review of external and internal inspections, and review of data obtained from operator training, evaluation, and certification. Many data and resources are available to help us understand analytical goals of new testing approaches, but we must begin to understand how better to gather and apply these data. Resources include but are not limited to College of American Pathologists Surveys, special studies such as CAP Q-Probes and data deriving from the Laboratory Management Improvement Program (LMIP), and information from the CAP Laboratory Accreditation Program. The use of all of these information sources will help us to avoid taking too narrow a view of analytical goals and how they should be evaluated; new technologies will require new approaches to goal setting and evaluation.

An example of the usefulness of these information sources is the report of Jones et. al. upon the report of the 1991 Q-Probe on bedside glucose monitoring; precision measurements based on 15,950 observations in 569 institutions were evaluated.[6] The authors concluded that programs demonstrated better performance if laboratorians were involved, appropriate operator training was instituted, if an internal quality comparison program was in place, and if an external proficiency testing program was used. On a global basis, this sort of observation is invaluable in helping us to assure quality performance.

Another tool is the CAP Laboratory

Deficiency	% of Surveyed Laboratories Deficient
In the absence of on-site supervisors, are the results of tests performed by personnel reviewed by the laboratory director, POCT section director, general supervisor, or the person in charge of the POCT section on the next routine working shift?	16.50
When applicable, are all patient results reported with accompanying reference (normal) ranges?	14.04
Are all reagents properly labeled with the following elements, as applicable and appropriate? 1. Content and strength, concentration or titer, 2. Storage requirements, 3. Date prepared or received, 4. Date placed in service, 5. Expiration date	13.75
Is linearity of the instruments/reagent system verified initially and at least semi-annually, or when calibration fails to meet the laboratory's acceptable limits?	13.05
Is there a documented system in operation to detect clerical errors, significant analytical errors, and unusual laboratory results?	9.36
Is quality control evaluated daily?	8.37
Is there documented evidence that quality control checks are performed on all tests each day of use with suitable positive and where appropriate, negative reference samples?	7.65
Is the laboratory enrolled in available CAP Surveys (Interlaboratory Comparison) program for the patient testing performed?	6.96
Is there evidence of corrective action when control results exceed defined tolerance limits?	6.90

Table 2. Inspection data from CAP Laboratory Accreditation Program, January through August, 1995. N = 589.

Accreditation Program; participation in laboratory accreditation activities as an inspector and as an inspected laboratory can be a very valuable experience, but what may we learn from a global evaluation of the data derived from the program, especially as regards point of care testing? Reviewing data from 589 laboratories inspected from January through August of 1995 shows that the most commonly cited deficiencies involve inadequate result review, failure to post normal ranges, failure to label reagents, and failure to check linearity (Table 2). Review of such data should help direct our efforts

for quality enhancement programs in testing at the bedside.

Hospitals may carry out their own programs relative to the monitoring and attainment of analytical goals, and indeed should do so as new and emerging technologies are encountered. Laposata conducted a series of elegant studies to show the usefulness of regular inspections of bedside glucose testing sites to maintaining quality results.[7] He has demonstrated that fast- paced clinical settings do more poorly overall with quality maintenance and that the most common quality assurance violation is failing to properly perform proficiency testing.

At Methodist Hospitals of Memphis, review of frequency of bedside blood glucose testing by analysts has shown wide disparity--some analysts perform only one or two tests per month, whereas others perform many hundreds. Such data are useful to help focus upon specific analysts who, through infrequency of testing, may require more intensive retraining or proficiency testing monitoring. In fact, as we attempt to "get the right answer" in an environment of improving technology and increasing numbers of less sophisticated analysts, reaching analytical goals may require that more emphasis be placed on monitoring the analyst than on monitoring the instruments and reagents. We may, for instance, develop proficiency testing paradigms in which relatively infrequent analysts are required to perform proficiency testing on a more frequent basis than are analysts who perform quality control and actual patient assays on a more frequent basis.

Summary and Conclusions

In summary, for adequate analytical goals to be set and monitored for new and emerging technologies, it will be critically necessary that we establish on the front end the need for such testing and that we are certain that new technology is really required to perform the task at hand. A current example is the observation that well-managed pneumatic tube systems to the central laboratory can replace point of care technology at a fraction of the cost and can maintain superior quality and turnaround times.[8] Another emerging theme in the diffusion of laboratory testing away from the central laboratory is the need to maintain excellent training and monitoring of analysts and, wherever possible, to keep the number of analysts to a minimum. Furthermore, new approaches to management of quality will be essential. We must devise practical quality control, proficiency testing, and training programs that are demonstrated to serve established analytical goals and, at the same time, to be cost-efficient.

Two emerging areas which are impacted by these issues are molecular pathology and in vivo patient testing. Each of these technologies represents high-cost testing areas for which we still must establish clinical and analytical goals. Through well conducted trials, we must decide how much quality management is sufficient to serve these goals and not attempt to apply old quality management paradigms to these technologies. Molecular pathology basically represents the challenge of how to benchmark non-numeric data, a challenge which has not yet been answered. In many ways, the failure of analytical goal setting in molecular pathology parallels a much older problem---that of analytical goal setting in microbiology. The challenge remains to broaden the concepts of goal setting beyond the establishment of numerical biological norms; we may need to strive much harder in

areas of epidemiological study to help understand what our goals of overall laboratory performance must be so that we serve the needs of whole populations of patients without spending resources needlessly. More and more, the analytical question which we answer may become "do I need to do this test at all?" rather than "how good an answer do I need to produce?"

An even more difficult emerging problem may be in the area of in vivo, continuous sensing technology. So-called nanotechnology is rapidly evolving, and very soon we will progress into an arena in which a considerable number of analytes may be evaluated on a patient in a real time, continuous monitoring mode. At this time, there still is some advantage since most of these technologies are still in a developmental or testing stage; there still may be time for thoughtful dialogue and a scientific approach to developing broad based analytical goals for these technologies. Laboratorians will need to resist the temptation to bind themselves to old approaches to goal setting, since in vivo technologies do not, at this time, conform very well to old laboratory paradigms of internal or external quality control by introducing a pseudo-sample. Indeed, for most in vivo technologies, the concept of an analyst is largely irrelevant. For this and other reasons, developers of in vivo technologies may be tempted to say that such technologies are not laboratory testing at all, but are merely "monitoring"; it therefore may be implied that such activities should not come under the scientific or regulatory purview of laboratory specialists. Such semantic dodging must be vigorously opposed, so that the patients of the future may have access in a systematic way to the most appropriate level of laboratory care. If we have learned anything from the experience of the implementing point of care laboratory testing in hospitals, it should be that when a disorganized, non-systematic approach is taken to the introduction of a new technology, it can take many years of effort to untangle the mess.

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